cancer using a tumor-localizing photosensitizer. *Cancer Letters* (1997) 111, 215-220; Sackmann M. Fluorescence diagnosis in GI endoscopy. Endoscopy (2000) 32, 977-985, and references therein].

The fluorescence endoscope consists of a small optical fiber probe inserted through the working channel of a conventional endoscope. Some fibers within this probe deliver the excitation light at 780 nm and others detect the fluorescence from the injected optical probe at 830 nm. The fluorescence intensity is displayed on a monitor.

Briefly, the CA20948 rat pancreatic tumor cells which are over-expressing somatostatin receptor are injected into the submucosa of a Lewis rat. The tumor is allowed to grow for two weeks. The rat is then anesthetized with xylazine : ketamine : acepromazine (1.5 : 1.5 : $0.5^{v/v}$) at 0.8 mL/kg via intramuscular injection. Cytate is injected in the tail vein of the rat and 60 minutes post-injection, the endoscope is inserted into the GI tract. Since cytate localizes in CA20948, the fluorescence intensity in the tumor is much higher than in the surrounding normal tissues. Thus, the relative position of the tumor is determined by observing the image on a computer screen.

Example 13

Imaging of Rat Pancreatic Acinar Carcinoma (CA20948) with Cytate 1 by Photoacoustic Technique

The photoacoustic imaging technique combines optical and acoustic imaging to allow better diagnosis of pathologic tissues. The preferred acoustic imaging method is ultrasonography where images are obtained by irradiating the animal with sound waves. The dual ultrasonography and optical tomography enables the imaging and localization of pathologic conditions (e.g., tumors) in deep tissues. To enhance the imaging, cytate is incorporated into

ultrasound contrast material. Methods for the encapsulation of gases in biocompatible shells that are used as the contrast material are described in the literature [Mizushige K., et al. Enhancement of ultrasound-accelerated thrombolysis by echo contrast agents: dependence on microbubble structure. *Ultrasound in Med. & Biol.* (1999), 25, 1431-1437]. Briefly, perfluorocarbon gas (e.g., perfluorobutane) is bubbled into a mixture of normal saline : propylene glycol : glycerol (7 : 1.5 : 1.5$^{v/v/v}$) containing 7 mg/ml of cytate : dipalmitoylphosphatidylcholine : dipalmitoylphosphatidic acid, and dipalmitoylphosphatidylethanolamine-PEG 5,000 (1 : 7 : 1 : 1 mole %). The CA20948 tumor bearing Lewis rat is injected with 1 ml of the microbubbles and the agent is allowed to accumulate in the tumor. An optical image is obtained by exciting the near infrared dye at 780 nm and detecting the emitted light at 830 nm, as described in Examples 9-11. Ultrasonography is performed by irradiating the rat with sound waves in the localized tumor region and detecting the reflected sound as described in the literature [Peter J. A. Frinking, Ayache Bouakaz, Johan Kirkhorn, Folkert J. Ten Cate and Nico de Jong. Ultrasond contrast imaging: current and new potential methods. *Ultrasound in Medicine & Biology* (2000) 26, 965-975].

Example 14

Photodynamic Therapy (PDT) and Localized Therapy of Rat Pancreatic Acinar Carcinoma (CA20948) with Cytate-PDT Agent Bioconjugates

The method for photodynamic therapy is well documented in the literature [Rezzoug H., et al. In Vivo Photodynamic Therapy with meso-Tetra (m-hydroxyphenyl)chlorin (mTHPC): Influence of Light Intensity and Optimization of Photodynamic Efficiency. *Proc.* SPIE (1996), 2924, 181-186; Stranadko E., et al. Photodynamic Therapy of Recurrent Cancer of Oral Cavity,

an Alternative to Conventional Treatment. *Proc.* SPIE (1996), 2924, 292-297]. A solution of the peptide-dye-phototherapy bioconjugate is prepared as described in Example 7 (5 µmol/mL of 15% DMSO in water, 0.5 mL) and is injected into the tail vein of the tumor-bearing rat. The rat is imaged 24 hours post injection as described in Examples 9-11 to localize the tumor. Once the tumor region is localized, the tumor is irradiated with light of 700 nm (which corresponds to the maximum absorption wavelength of HPPH, the component of the conjugate that effects PDT). The energy of radiation is 10 J/cm^2 at 160 mW/cm^2. The laser light is transmtited through a fiber optic, which is directed to the tumor. The rat is observed for 7 days and any decrease in tumor volume is noted. If the tumor is still present, a second dose of irradiation is repeated as descried above until the tumor is no longer palpable.

For localized therapy, a diagnostic amount of cytate (0.5 mL/0.2 Kg rat) is injected into the tail vein of the tumor-bearing rat and optical images are obtained as described in Examples 9-11. A solution of the peptide-dye-phototherapy bioconjugate is prepared as described in Example 7 (5 µmol/mL of 15% DMSO in water, 1.5 mL) and is injected directly into the tumor. The tumor is irradiated as described above.

Example 15

Photodiagnosis with Atherosclerotic Plaques and Blood Clots

A solution of a peptide-dye-bioconjugate for targeting atherosclerotic plaques and associated blood clots is prepared as described in Example 7. The procedure for injecting the bioconjugate and subsequent localization and diagnosis of the plaques and clots is performed as described in Example 14.